EXHIBIT A

DAVID L. PEARLE, M.D.

PERSONAL INFORMATION

HOME ADDRESS:	8709 Bellwood Road Bethesda, Maryland 20817
BUSINESS TELEPHONE:	(202) 444-8833 / (202) 444-1839 FAX
EMAIL ADDRESS:	[redacted]
BIRTH DATE:	September 3, 1942
BIRTHPLACE:	Pittsburgh, Pennsylvania
CITIZENSHIP:	U.S.A.
MARITAL STATUS:	Married, two children

EDUCATION

1964 1965	B.A., Amherst College, cum laude Amherst, Massachusetts
1968	M.D., Harvard Medical School, Boston, Massachusetts

TRAINING/ PROFESSIONAL POSITIONS

1968-1969	Internship in Medicine, New York Hospital
1969-1970	Residency in Medicine, New York Hospital
1970-1972	Commissioned Officer, Public Health Service (Military Service) Clinical Instructor of Medicine, George Washington University Hospital, Washington, DC
1972-1974	Cardiology Fellow, Georgetown University Hospital, Washington, DC
July 1974-January 1975	1970 Hemodynamics Fellow, Washington Veterans Administration Hospital Washington, DC

February 1975-June 1975	Staff Cardiologist, Washington Veterans Administration Hospital, Washington, DC
July 1975-March 1983	Staff Cardiologist, Georgetown University Hospital, Washington, DC Assistant Director, Coronary Care Unit, Georgetown University Hospital, Washington, DC
April 1983-June 1989	Co-Director, Medical Special Care Unit, Georgetown University Hospital, Washington, DC
April 1987-1989	Transplant Cardiologist, Georgetown University Hospital, Washington, DC
July 1988-January 1993	Acting Chief, Division of Cardiology, Georgetown University Hospital, Washington, DC
1990-2002	Director, Georgetown Heart Failure Service
October 1995-Present	Director, Coronary Care Unit, Georgetown University Hospital, Washington, DC

APPOINTMENTS

1970	Clinical Instructor of Medicine, George Washington University Hospital, Washington, DC
1974	Instructor of Medicine, Georgetown University Hospital, Washington, DC
1975	Assistant Professor of Medicine (Cardiology), Georgetown University Hospital, Washington, DC
1976	Assistant Professor of Medicine and Pharmacology, Georgetown University Hospital, Washington, DC
1980	Associate Professor of Medicine and Pharmacology, Georgetown University Hospital, Washington, DC (Tenured)
1991	Professor of Medicine, Georgetown University Hospital, Washington, DC (Tenured)
2000	Professor of Medicine, Medstar Georgetown University Hospital, Washington, DC

CERTIFICATION

1974	American Board of Internal Medicine
1975	American Board of Internal Medicine, Subspecialty of Cardiovascular Diseases
2000	American Board of Internal Medicine, Subspecialty of Interventional Cardiology

LICENSURE

New York, 1970
District of Columbia, 1972
Virginia, 1995
Maryland, 2003

AWARDS

Special Clinical Fellowship, Washington Heart Association, 1972-1973
Donald Zucker Visiting Professor, Cornell/New York Hospital, 1991
Vicennial Medal, Georgetown University, 1994
Distinguished Alumnus Award, W. Proctor Harvey Society, 1994
Washingtonian Magazine, Top Doctors, 1991-2005
America's Top Physicians, Consumers Research Council of America, 2004-2005

PROFESSIONAL SOCIETIES

* American Heart Association, National's Capital Affiliate, President 1984-1986
* Intersociety Commission for Heart Disease Resources
* Fellow, American College of Cardiology
* Fellow, American Heart Association, Council on Clinical Cardiology
* Medical Society of the District of Columbia
* Fellow, American Federation for Clinical Research
* Fellow, Society for Cardiac Angiography

HOSPITAL AND MEDICAL CENTER COMMITTEES

* Chairman, CPR Committee, 1976-1985
* Intern Selection Committee, Department of Medicine, 1976-1984
* Institutional Review Board, 1978-1982
* Search Committee, Pediatrics Chair, 1988
* University Fiscal Affairs Committee, 1990
* Faculty Senate, 1988-1991
* Hospital Capital Equipment Committee, 1989-1993
* Search Committee, Anesthesia Chair, 1988
* Medical Center Bylaws and Governance Committee, 1990
* Department of Medicine Billing Committee, 1992-1996

* University Faculty Grievance Committee, 1998-2000
* Chairman, CPR Committee, 1999-Present
* Division of Cardiology
    * Executive Committee, 1992
    * Billing Committee, Chair, 1992
    * Strategic Planning Committee, 1992
* Pharmacy and Therapeutics Committee, 1999- Present

RESEARCH GRANTS AWARDED

1. ÒChlordiazepoxide for Ventricular ArrhythmiasÓ
   American Heart Association, NationÕs Capital Affiliate-1975

2. ÒNifedipine, Angina, and Myocardial Infarction StudyÓ
   Pfizer laboratories-1979-1982
   $72,635
   Principal Investigator: David L. Pearle, MD

3. ÒNifedipine: To Determine Efficacy in Management of Angina PectorisÓ
   Pfizer laboratories-1979-1982
   Principal Investigator: David L. Pearle, MD

4. ÒOpen, Multi Center Trial of Ibopamine Hydrochloride in Patients with Congestive Heart Failure: Long Term SafetyÓ
   Smith, Kline, and French Laboratories- 1984-1987
   $176,490
   Principal Investigator: David L. Pearle, MD

5. ÒDouble Blind, Placebo-Controlled, Multi Center Trial of Ibopamine in Patients with Congestive Heart Failure: Invasive Evaluation of Hemodynamic Parameters and Exercise TestingÓ
   Smith, Kline, and French Laboratories- 1985-1987
   $176,490
   Principal Investigator: David L. Pearle, MD

6. ÒOpen Safety Trial of Ibopamine with Captropril and Hydralazine: Acute Hemodynamic Study with Short Term Chronic DosingÓ
   Smith, Kline, and French Laboratories- 1985-1987
   $59,700
   Principal Investigator: David L. Pearle, MD

7. ÒAn Optional, Open, Long Term Study of the Effects of Flosequinan 75, 100, or 150 mg q.d. on Safety, Tolerance, Survival Time and Disease Symptomatology in Congestive Heart Failure Patients Randomized to the BP1 919 Double Blind StudyÓ
   The Boots Company, U.S.A., Inc.
   $25,000
   Principal Investigator: David L. Pearle, MD

8. ÒAn Optional, Open-Label, Long Term Study of the Effects of Flosequinan 100 mg Once a Day (with 150 mg/ 100 mg/ 75 mg/ 50 mg up or down titration) on Safety, Tolerability, Survival Time and Disease Symptomatology in Congestive Heart Failure Patients Who Have Participated in BPI-934Ó
   The Boots Company, U.S.A., Inc.
   $48,000
   Principal Investigator: David L. Pearle, MD

9. ÒModern Approach to the Treatment of Hypertension Multi-Center Study (MATH)Ó
   Pfizer, Inc.
   $4,000
   Principal Investigator: David L. Pearle, MD

10. ÒAn Open-Label, Compassionate-Use, Long Term Study to Evaluate the of Repeated Daily Oral Doses of Flosequinan in Patients with Congestive Heart FailureÓ
The Boots Company, U.S.A., Inc.
$ N/a
Principal Investigator: David L. Pearle, MD

11. ÒA Multi-Center, Double Blind, Placebo-Controlled Study of the Effects of Manoplax (Flosequinan) 75 mg Twice Daily or 100 mg Once Daily on Duration of Exercise Treadmill Testing and Disease Symptoms for Up to 12 Weeks in Symptomatic Congestive Heart Failure Patients on Angiotensin Converting Enzyme Inhibitors (ACEIs)
The Boots Company, U.S.A., Inc.
$180,000
Principal Investigator: David L. Pearle, MD

12. "An Invasive Hemodynamic Study of the Effects, Safety, and Tolerability of 75 mg Twice Daily, 100 mg Once Daily, or 150 mg Once Daily Manoplax (Flosequinan) in New York Heart Association Class III or IV Congestive Heart Failure Patients Uncontrolled by Angiotensin Converting Enzyme Inhibitors (ACEIs) and DiureticsÓ
The Boots Company, U.S.A., Inc.
$420,000
Principal Investigator: David L. Pearle, MD

13. ÒA Double Blind, Placebo-Controlled, Parallel Group, Invasive Hemodynamic Study with Manoplax (Flosequinan) 75 mg Twice Daily, or 150 mg Once Daily for Two Weeks in New York Heart Association Class III and IV Congestive Heart Failure Patients Symptomatic on Angiotensin Converting Enzyme Inhibitors, BPI 993Ó
The Boots Company, U.S.A., Inc.
$420,700
Principal Investigator: David L. Pearle, MD

14. ÒAn Open-Label, Long Term Study of the Effects of Manoplax (Flosequinan) 50 mg b.i.d. (with 75 mg b.i.d. upward titration or 25 mg b.i.d. downward titration) on Safety, Tolerability, Survival Time and Disease Symptomatology in Congestive Heart Failure Patients Who Have Participated in BPI 993Ó
The Boots Company, U.S.A., Inc.
$89, 800
Principal Investigator: David L. Pearle, MD

15. ÒU.S. Thrombolysis RegistryÓ
Medical Research International
$ N/a
Principal Investigator: David L. Pearle, MD

16. ÒEffects of Aminodipine on Exercise Tolerance and Safety in Patients with Chronic, Symptomatic (New York Heart Association Class II-IV) Heart Failure Receiving a Combination of Angiotensin Converting Enzyme Inhibitors, Digoxin, and DiureticsÓ
Pfizer Laboratories
Funded at $59,368 Current available $11,887 (funds stilled owed)
Principal Investigator: David L. Pearle, MD

17. ÒLong Term Double Blind Evaluation of the Safety of Amlodopine in Patients with Heart Failure (175E)Ó
Pfizer Laboratories
Funded at $5,00 Current available- $4,832
Principal Investigator: David L. Pearle, MD

18. ÒA Double Blind Multi Center Comparison of Oral Carvedilol b.i.d. with Placebo in the Treatment of Patients with Congestive Heart Failure, New York Heart Association Class III-IV (221)Ó
Smith, Kline, and Beecham
Funded at $24,855 (Projected-$72,000) Current available $2,622
Principal Investigator: David L. Pearle, MD

19. ÒA Six Month Double Blind Multi Center Comparison of Oral Carvedilol b.i.d. with Placebo in the Treatment of Patients with Congestive Heart Failure, New York Heart Association Class III-IV (239)Ó
Smith, Kline, and Beecham 1992
Funded at $5,145 (Projected-0) Current available $9,606
Principal Investigator: David L. Pearle, MD

20. ÒA Two Year, Open Label Multi Center, Safety Study of Twice Daily Oral Carvedilol in Patients with New York Heart Association Class I-IV Congestive Heart Failure (Extension)Ó
Sponsor: Smith Kline and Beecham
Total Grant Amount: $22,760
Amount Funded as of June 1995: $8,535 (Funds due)
Status: Active
Principal Investigator: David L. Pearle, MD

21. Achieve Congestive Heart Failure Investigation and Economic Variable Evaluation with Accupril
Sponsor: Park Davis
Total Grant Amount: $235/pt.
Amount Funded as of June 1995: $1,250
Status: Active
Principal Investigator: David L. Pearle, MD

22. A Multi Center Double Blind Randomized Parallel Design, Pilot Study to Evaluate the Safety and Tolerability of Losartan Administered in Addition to Enalapril in Patients with Heart Failure Treated Previously with ACE Inhibitors
Sponsor: Merck and Co.
Total Grant Amount: $45,000
Amount Funded as of June 1995:0
Status: Active
Principal Investigator: David L. Pearle, MD

23. An Open Label Evaluation of Carvedilol in Patients with Chronic Congestive Heart Failure New York Heart Association Class II-IV
Sponsor: Smith Kline and Beecham
Total Grant Amount: $500/pt.
Amount Funded as of June 1995: 0
Status: Active
Principal Investigator: David L. Pearle, MD

24. A Six-Month Double Blind, Multi Center Evaluation of Oral Carvedilol b.i.d. Compared with Placebo in Patients with New York Heart Association Class III-V
Sponsor: Smith Kline and Beecham
Total Grant Amount: $82,850
Amount Funded as of June 1995: $5,145
Status: Closed
Principal Investigator: David L. Pearle, MD

25. A 12-Month Double Blind, Multi Center Comparison of Oral Carvedilol b.i.d. with Mild Congestive Heart Failure New York Heart Association Class II
Sponsor: Smith Kline and Beecham
Total Grant Amount: $53,795.
Amount Funded as of June 1995: $9,606
Status: Closed
Principal Investigator: David L. Pearle, MD

26. BEST Beta-Blocker Evaluation of Survival Trial: Bucindolol
Sponsor: National Heart, Lung, and Blood Institute, Va. Coop.
Total Grant Amount: $120,000
Amount Funded as of June 1995: 0
Status: Active
Principal Investigator: David L. Pearle, MD

27. PRAISE II Prospective Randomized Amlodipine Survival Evaluation
Sponsor: Pfizer, Inc.
Total Grant Amount: to be negotiated
Amount Funded as of June 1995: 0
Status: Active
Principal Investigator: David L. Pearle, MD

28. VEST Vesnarinone Trial
Sponsor: Otsuka Pharmaceuticals.
Total Grant Amount: $78,750
Amount Funded as of June 1995: 0
Status: Active
Principal Investigator: David L. Pearle, MD

29. The Effect of RO-40 on Exercise Treadmill Test Duration and Al Cause Mortality in Patients with Chronic Congestive Heart Failure New York Heart Association Class II-V Treated for Approximately 3-Years
Sponsor: Hoffman LaRoche
Total Grant Amount: $128,292
Amount Funded as of April 1995: 0
Status: Closed
Principal Investigator: David L. Pearle, MD

Abstracts

Pearle, D.L., Corr, P.B., and R.A Gillis. Influences of site of cardiovascular changes induced by coronary ligation. Federal Process 33:162, 1974

Pearle, D.L., and R.A Gillis. Effects of digitalis on the response of ventricular pacemakers to sympathetic nerve stimulation. Am J Cardiology 3:162, 1974.

Pearle, D.L., T. Hoekman, K.M. Kent, and R.A Gillis. Pharmacological analysis of a cardiac sympathetic neural response resistant to beta-adrenergic blockage. Circulation 50: 111-37, Supplement III, 1974.

Corr, P.B., D.L., Pearle, and R.A Gillis. Occlusion site as a determinant of the deleterious effects of atropine in experimental myocardial infarction. Am J Cardiology 35:129, 1975.

Pearle, D.L., Williford, and R.A Gillis. Comparison of practolol and propranolol on coronary occlusion-induced ventricular fibrillation. Am J Cardiology 41:399, 1978.

Chizner, M.D., D.L., Pearle, and A.C. deLeon Jr. Natural history of aortic stenosis in adults. Chest 74:3322, 1978.

Pearle, D.L., J. Dias Souza, and R.A Gillis. Comparative vagolytic effects of procainamine and n-acetylprocainamide in the dog. Clinical Research 27:139 A, 1979.

Alexander, G.J., J. Dias Souza, S.A. Segal, D.L., Pearle and R.A Gillis. Experimental coronary artery spasm: Prevention by nisoldipine and nifedipine by not by verapamil. Clinical Research, April 1983.

Muller, J., J. Morrison, P. Stone, R. Rude, B. Rosner, R. Roberts, D.L., Pearle, Z. Turi, J. Schneider, D. Serfas, C. Hennekens, E. Braunwald. Nifedipine therapy for threatened and acute myocardial infarction: A randomized double blind comparison. Circulation 68:111-120, 1983.

Muller, J., Z. Turi, D.L., Pearle, J. Schneider, D. Serfas, J. Morrison, P. Stone, R. Rude, B. Rosner, E. Scheiner, R. Roberts, B. Sovel, C. Hennekens, E. Braunwald. Nifedipine vs. conventional therapy for unstable angina pectoris: A randomized double blind comparison. JACC 3: 551, 1984.

Gatti, P.J., J. Dias Souza, J.A. Quest, P. Hamosh, D.L., Pearle, R.A Gillis. Ventricular tachyarrhythmias induced by exciting cell bodies in the area postrema of the cat. Clinical Research 32:167A, 1984.

Satler, L.F., D.L., Pearle, A.A. Del Negro, K.M. Kent, S. Levine, C.E. Rackley. Reason for low hospital mortality after thrombolysis. Clinical Research 32:681A, 1984.

Satler, L.F., C.E. Green, D.L., Pearle, R.S. Pallas, A.A. Del Negro, K.M. Kent, R.D. Fletcher, C.E. Rackley. The importance of metabolic support of the left ventricle after coronary thrombolysis. JACC 5:413, 1985.

Krucoff, M.W., C.E. Green, L.F. Satler, F.C. Miller, R.S. Pallas, D.L., Pearle, K.M. Kent, R.D. Fletcher, C.E. Rackley. ST segment monitoring as a predictor of thrombolysis in acute myocardial infarction. JACC 5:522, 1985.

Pallas, R.S., L.F. Satler, D.L., Pearle, K.M. Kent, A.A. Del Negro, C.E. Green, C.E. Rackley. Clinical course of patients undergoing emergency angiography during acute myocardial infarction. Clinical Research 32:831A, 1984.

Pearle, D.L., L.F. Satler, K.M. Kent, A.A. Del Negro, N.M. Katz, R.B. Wallace, C.E. Rackley. The financial costs of intra coronary thrombolysis. Clinical Research 32:83A, 1984.

Satler, L.F., N.M. Katz, K.M. Kent, D.L., Pearle, A.A. Del Negro, C.E. Rackley, R.B. Wallace. Short term mortality for coronary revascularization in the high-risk patient. Clinical Research 32:832A, 1984.

Krucoff, M.W., C.E. Green, D.L., Pearle, F.C. Miller, R.S. Pallas, A.A. Del Negro, K.M. Kent, R.D. Fletcher, C.E. Rackley. Successful thrombolysis predicted by ST segment monitoring. Clinical Research 32:830A, 1984.

Krucoff, M.W., C.E. Green, L.F. Satler, F.M. Miller, R.S. Pallas, D.L., Pearle, R.D. Fletcher, C.E. Rackley. The use of Holter monitoring to identify subtotal coronary occlusions. Clinical Research 32:675A, 1984.

Satler, L.F., C.E. Green, D.L., Pearle, S. Levine, A.A. Del Negro, K.M. Kent, C.E. Rackley. The effects of glucose-insulin-potassium on left ventricle function after coronary thrombolysis. Clinical Research 32:681A, 1984.

Satler, L.F., N.M. McNamara, R.S. Pallas, K.M. Kent, D.L., Pearle, C.E. Green, A.A. Del Negro, C.E. Rackley. Intravenous streptokinase for acute myocardial infarction during emergency ambulance transfer. Clinical Research 32:682A, 1984.

Pallas, R.S., C.E. Green, L.F. Satler, D.L., Pearle, A.A. Del Negro, K.M. Kent, S. Levine, C.E. Rackley. Coronary collateral incidence and its association with multi vessel disease during acute myocardial infarction. Clinical Research 32:679A, 1984.

Satler, L.F., C.E. Green, D.L., Pearle, S. Levine, A.A. Del Negro, K.M. Kent, C.E. Rackley. The beneficial effects of glucose-insulin-potassium therapy during acute thrombolysis. Circulation 70:11-153, 1984.

Satler, L.F., W.J. Rogers, K.M. Kent, L.M. Fox, H. A. Goldstein, R.S. Pallas, A.A. Del Negro, D.L., Pearle, C.E. Rackley. Demonstration of salvaged myocardium after successful coronary reperfusion. Clinical Research 33:747A, 1985.

Fletcher, A.M., L.F. Satler, R.S. Pallas, S.W. Ahemed, K.M. Kent, D.L., Pearle, C.E. Rackley. Therapy and cost in patients over 65 years of age hospitalized for acute myocardial infarction. Clinical Research 33:740A, 1985.

Satler, L.F., R.S. Pallas, C.E. Green, D.L., Pearle, A.A. Del Negro, K.M. Kent, N.M. Katz, R. B. Wallace, C.E. Rackley. Frequency of coronary angioplasty and coronary bypass after thrombolytic therapy. Clinical Research 33:224A, 1985.

McNamara, N.M., L.F. Satler, R.S. Pallas, C.E. Green, D.L., Pearle, A.A. Del Negro, K.M. Kent, C.E. Rackley. Bleeding complications of thrombolytic therapy. Clinical Research 33:211A, 1985.

Satler, L.F., C.E. Green, R.S. Pallas, D.L., Pearle, A.A. Del Negro, C.E. Rackley, K.M. Kent. Demonstration of salvaged myocardium after fibrinolytic therapy with coronary angioplasty. Clinical Research 33:224A, 1985.

Pallas, R.S., D.L., Pearle, L.F. Satler, C.E. Green, A.A. Del Negro, K.M. Kent, C.E. Rackley. Angiographic characteristics of stenosis in the infarct-related vessel after streptokinase. Clinical Research 33:224A, 1985.

Satler, L.F., C.E. Green, R.S. Pallas, D.L., Pearle, A.A. Del Negro, C.E. Rackley, K.M. Kent. Ischemia during angioplasty after streptokinase: A marker of salvaged myocardium. Clinical Research 33:747A, 1985.

Lavelle, J.P., M.L. Leitschuh, L.F. Satler, R.S. Pallas, C.E. Green, A.A. Del Negro, D.L., Pearle, C.E. Rackley, K.M. Kent. Short and long term follow-up for coronary angioplasty in acute myocardial infarction. Clinical Research 33:744A, 1985.

McNamara, N.M., L.F. Satler, S. W. Ahemed, A.A. Del Negro, R.S. Pallas, D.L., Pearle, K.M. Kent, C.E. Rackley. Hemorrhagic problems associated with thrombolytic therapy for acute myocardial infarction. Clinical Research 33:745A, 1985.

Satler, L.F., R.S. Pallas, C.E. Green, D.L., Pearle, A.A. Del Negro, K.M. Kent, N.M. Katz, R.B. Wallace, C.E. Rackley. Hospital course after streptokinase: Frequency of coronary angioplasty and coronary bypass. Clinical Research 33:747A, 1985.

Pearle, D.L., R.S. Pallas, L.F. Satler, C.E. Green, A.A. Del Negro, K.M. Kent, C.E. Rackley. The incidence of normal or near-normal infarct-related vessels after streptokinase for myocardial infarction. Clinical Research 33:173A, 1986.

Fletcher, A.M., L.F. Satler, R.S. Pallas, C.E. Green, D.L., Pearle, A.A. Del Negro, K.M. Kent, C.E. Rackley. Final treatment after thrombolytic therapy for infarction. Clinical Research 34:169A, 1986.

Lavelle, J.P., L.F. Satler, R.S. Pallas, C.E. Green, A.A. Del Negro, D.L., Pearle, C.E. Rackley, K.M. Kent. Coronary angioplasty for acute myocardial infarction: short and long term follow up. Clinical Research 34:172A, 1986.

Pallas, R.S., L.F. Satler, D.L., Pearle, C.E. Green, A.A. Del Negro, K.M. Kent, C.E. Rackley. Infarct vessel residual stenosis and feasbility of coronary angioplasty after streptokinase. Clinical Research 34:173A, 1986.

McNamara, N.M., L.F. Satler, S.W. Ahmed, A.A. Del Negro, R.S. Pallas, D.L., Pearle, K.M. Kent, C.E. Rackley. Bleeding complication after streptokinase for acute myocardial infarction. Clinical Research 34:209A, 1986.

Satler, L.F., K.M. Kent, L.M. Fox, H.A. Goldstein, W.J. Rogers, R.S. Pallas, A.A. Del Negro, D.L., Pearle, C.E. Rackley. The effects of thrombolytic therapy on inotropic contractile reverse. Clinical Research 34:209A, 1986.

Fletcher, A.M., L.F. Satler, R.S. Pallas, C.E. Green, D.L., Pearle, A.A. Del Negro, K.M. Kent, C.E. Rackley. Hospital therapy after streptokinase infusion for infarction. Clinical Research 34:298A, 1986.

Pallas, R.S., L.F. Satler, D.L., Pearle, C.E. Green, A.A. Del Negro, K.M. Kent, C.E. Rackley. Feasbility for coronary angioplasty after thrombolysis. Clinical Research 34:334A, 1986.

McNamara, N.M., L.F. Satler, S.W. Ahmed, A.A. Del Negro, R.S. Pallas, D.L., Pearle, K.M. Kent, C.E. Rackley. Bleeding with streptokinase: Implications for therapy. Clinical Research 34:325A, 1986.

Packer, M., K.A. Narahara, U. Elkayam, J.M. Sullivan, D.L., Pearle, B.M. Massie, M.A. Creager (on behalf of the Principal Investigators of the REFLECT study. Mount Sinai School of Medicine, New York, NY). Randomized, Multi Center, double blind, placebo-controlled study of the efficacy of flosequinan, a new, long-acting vasodilator drug in patients with chronic heart failure. Supplement to Circulation 82:111-323, October, 1990.

Publications

Gillis, R.A., D.L., Pearle, and T. Hokeman. Failure of beta adrenergic receptor blockage to prevent arrhythmias induced by cardiac sympathetic nerve stimulation.
Science 185:70, 1974.

Pearle, D.L., and R.A. Gillis. Effects of digitalis on the response of the ventricular pacemaker to sympathetic neural stimulation and to isoproterenol.
American Journal of Cardiology 34:704, 1974.

Gillis, R.A., D.L., Pearle, and B. Levitt. Digitalis: A neuro-excitatory drug. Circulation 52:379, 1975.

Corr, P.B., D.L., Pearle, and R.A. Gillis. Coronary occlusion site as a determinant of the cardiac rhythm effects of atropine and vagotomy.
American Heart Journal 92:741, Dec. 1976.

Corr, P.B., D.L., Pearle, J.R. Hinton, W.C. Roberts, and R.A. Gillis. Site of myocardial infarction-a determinant of the cardiovascular changes induced in the cat by coronary occlusion. Circulation Research 39:840, Dec. 1976.

Gillis, R.A., P.B. Corr, D.G. Pace, D.E. Evans, J. A. DiMicco, and D.L., Pearle. Role of the nervous system in experimentally induced arrhythmias. Cardiology 61:37, 1976.

DiMicco, J.A., R. Prestel, D.L., Pearle, and R.A. Gillis. Mechanism of cardiovascular changes produced in cats by activation of the central nervous system with picrotoxin.
Circulation Research 41:446, Oct. 1977.

Pearle, D.L., D.J. Williford, and R.A. Gillis. Superiority of protocol versus propranolol in protection against ventricular fibrillation induced by coronary occlusion. American Journal of Cardiology 42:960, 1978.

Pearle, D.L. Clinical experience with nifedipine for coronary artery spasm. Medical Times 107:12, Dec. 1979.

Chizner, M.D., D.L., Pearle, and A.C. deLeon, Jr. Natural history of aortic stenosis in adults.
American Heart Journal 99:419-424, April, 1980.

Segal, S.A., D.L., Pearle, and R.A. Gillis. Coronary spasm produced by picrotoxin in cats.
European Journal of Pharmacology 76: 447-451, 1981.

Pearle, D.L., J. Dias Souza, and R.A. Gillis. Comparative vagolytic effects of procainamide and n-acetylprocainamide in the dog.
Journal of Cardiovascular Pharmacology, 5:450-453, 1983.

Pearle, D.L. Clinical experience with nifedipine for coronary artery spasm.
Resident & Staff Physician 26:4, 1979.

Muller, J.E., Z.G. Turi, D.L., Pearle, J.F. Schneider, D.H. Serfas, J. Morrison, P.H. Stone, R.E. Ruide, B. Rosner, B.E. Sobel, C. Tate, E. Scheiner, R. Roberts, C.H. Hennekens, and E. Braunwald. Nifedipine and conventional therapy for unstable angina pectoris: A randomized double blind comparison. Circulation 69:728-739, 1984.

Muller, J.E., J. Morrison, P.H. Stone, R.E. Rude, B. Rosner, R. Roberts, D.L., Pearle, Z.G. Turi, J.F. Schneider, D.H. Serfas, C. Tate, E. Scheiner, , B.E. Sobel, C.H. Hennekens, and E. Braunwald. Nifedipine therapy for patients with threatened and acute myocardial infarction: A randomized, double blind, placebo-controlled comparison. Circulation 69:740-747, 1984.

Satler, L.F., S. Levine, A.A. Del Negro, D.L., Pearle, K.M. Kent, and C.E. Rackley. Non-surgical coronary reperfusion in evolving myocardial infarction. Advances in Internal Medicine 30:231-242, 1984.

Satler, L.F., D.L., Pearle, S. Levine, C.E. Green, A.A. Del Negro, and C.E. Rackley. Aortic dissection masquerading as acute myocardial infarction: Implication for thrombolytic therapy without cardiac catherization. American Journal of Cardiology 54:1134-1135, Nov 19984.

Pearle, D.L. Nifedipine in acute myocardial infarction. American Journal of Cardiology 54:21 E. 1984.

Pearle, D.L. Ischemia Heart Disease: Clinical update. Monograph. Home Study Assessment. American Academy of Family Physicians 66, 1984.

Satler, L.F., D.L., Pearle, S. Levine, C.E. Green, A.A. Del Negro, K.M. Kent, and C.E. Rackley. Changing concepts and treatment of unstable myocardial ischemia. Primary Cardiology 10:88-94, 1984.

Gillis, R.A., B.I. Lee, and D.L., Pearle. Practical pharmacology of anti-ischemic agents. Consultant, 25-27, 68-92, April 1985.

Satler, L.F., C.E. Rackley, D.L., Pearle, R.D. Fletcher, and A.A. Del Negro. Total inhibition of a physiologic pacing system due to antipacemaker-mediated tachycardiac mode. PACE 8:806-810, 1985.

Satler, L.F., K.M. Kent, C.E. Green, D.L., Pearle, R.S. Pallas, A.A. Del Negro, and C.E. Rackley. Thrombolysis in acute myocardial infarction. In Advances in Critical Care Cardiology. Philadelphia: F.A. Davis Company, 1986:39-52.

Rackley, C.E., L.F. Satler, D.L., Pearle, A.A. Del Negro, R.S. Pallas, and K.M. Kent. The use of hemodynamic measurements for the management of acute myocardial infarction. . In Advances in Critical Care Cardiology. Philadelphia: F.A. Davis Company, 1986:3-15.

Satler, L.F., C.E. Rackley, C.E. Green, R.S. Pallas, D.L., Pearle, A.A. Del Negro, and K.M. Kent. Ischemia during angioplasty after streptokinase: A marker of myocardial salvage. American Journal of Cardiology 56:749-752, 1985.

Krucoff, M.W., C.E. Green, L.F. Satler, F.C. Miller, R.S. Pallas, K.M. Kent, A.A. Del Negro, D.L., Pearle, R.D. Fletcher, and C.E. Rackley. Noninvasive detection of coronary artery patency using continuos ST segment monitoring. American Journal of Cardiology 57:916-922, 1986.

Satler, L.F., K.M. Kent, L.M. Fox, C.E. Green, W.J. Rogers, R.S. Pallas, A.A. Del Negro, D.L., Pearle, and C.E. Rackley. The assessment of contractile reserve after thrombolytic therapy for acute myocardial infarction. American Heart Journal 111:821-825, 1986.

Rackley, C.E., L.F. Satler, M.W. Krucoff, R.S. Pallas, D.L., Pearle, A.A. Del Negro, and K.M. Kent. Future directions for the diagnosis and treatment of acute myocardial infarction. In: R.H. Cox, ed. Acute Myocardial Infarction. New York: Praeger Publisher, Inc. in press.

Pearle, D.L. and C.E. Rackley. Beta-blockers and calcium channel blocking agents in acute myocardial infarction. In Advances in Critical Care Cardiology. Philadelphia: F.A. Davis Company, 1986:29-38.

Katz, N.M., T.E. Kubanick, S:W. Ahmed, C.E. Green, D.L., Pearle, L.F. Satler, C.E. Rackley, and R.B. Wallace. Determinants of cardiac failure after coronary bypass surgery within 30 days of acute myocardial infarction.

Satler, L.F., C.E. Green, K.M. Kent, R.S. Pallas, D.L., Pearle, and C.E. Rackley. Metabolic support during coronary reperfusion. American Heart Journal 114:54-58, 1987.

Satler, L.F., R.S. Pallas, O.B. Bond, C.E. Green, D.L., Pearle, G.L. Schaer, K.M. Kent, and C.E. Rackley. Assessment of the residual coronary arterial stenosis after thrombolytic therapy during acute myocardial infarction. American Journal of Cardiology 59:1231-1233, 1987.

Satler, L.F., C.E. Green, N.M. McNamara, J.P. Lavelle, R.S. Pallas, D.L., Pearle, K.M. Kent, and C.E. Rackley. Late angiographic follow-up after successful thrombolysis and angioplasty. American Journal of Cardiology 60:210-213, 1987.

Bowman, M.A., and D.L., Pearle. Changes in drug prescribing patterns related to commercial company funding of continuing medical education. Journal of Continuing Education Health Professional 8:13-20, 1988.

Pearle, D.L., Calcium antagonist in acute myocardial infarction. American Journal of Cardiology 61:22B-25B, 1988.

Satler, L.F., D.L., Pearle, and C.E. Rackley. Reduction in coronary heart disease: Anatomical considerations. Clinical Cardiology 12:422-426, 1989.

Katz, N., P. Pierce, R. Anzeck, M. Visner, H. Canter, M. Forgh, D.L., Pearle, C.M. Tracy, and A. Rahman. Liposomal amphotericin B for treatment of pulmonary aspergillosis in a heart transplant patient. The Journal of Heart Transplantation, 9:14-17, Jan/Feb, 1990.

Pearle, D.L., Pharmacological management of ischemic heart disease with B-blockers and calcium channel blockers.
American Heart Journal 120:739-742, September, 1990.

Packer, M., Narahara K.A., Elkayam U., Sullivan J.M., D.L., Pearle, Massie, B.M., and Creager, M.A. Double blind, placebo-controlled study of the efficacy of flosequinan in patients with chronic heart failure.
Journal American College of Cardiology, 22(1):65-72, July, 1993.

Coughlin, S.S., D.L., Pearle, K.L. Baughman, A. Wasserman, and M.C. Tefft Diabetes mellitus and the risk of idiopathic dilated cardiomyopathy. Annals of Epidemiology, 4:45-52, 1994.

Pearle, D.L. and DiBlanco, R. Clinical Approach to Heart Failure in Classic Teachings in Teachings in Clinical Cardiology, Laennec Publishing, 1996.

Antman EM., Anbe DT; Armstrong PW; Bates ER; Green LA; Hand M; Hochman JS; Krumholz HM; Kushner FG; Lamas GA; Mullany CJ; Ornato JP; Pearle DL; Sloan MA; Smith SC Jr; ACC/AHA Guidelines for the Management of Patients With ST- Elevation Myocardial infarction-Executive Summary. J AM Coll Cardiol 2004;44: 671-719.

Antman EM; Anbe DT; Armstrong PW; Bates ER; Green LA; Hand M; Hochman JS; Krumholz HM; Kushner FG; Lamas GA; Mullany CJ; Ornato JP; Pearle DL; Sloan MA; Smith SC JR; ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction Executive Summary. Circulation. 2004;110:588-636

EXHIBIT B

ELSEVIER

Journal of Biomechanics 38 (2005) 1574–1581

JOURNAL OF BIOMECHANICS

www.elsevier.com/locate/jbiomech
www.JBiomech.com

Cardiovascular stent design and vessel stresses: a finite element analysis

C. Lally[a], F. Dolan[b], P.J. Prendergast[a,*]

[a]*Centre for Bioengineering, Department of Mechanical Engineering, Trinity College, Dublin 2, Ireland*
[b]*Medtronic Vascular, Parkmore Industrial Estate, Galway, Ireland*

Accepted 30 July 2004

Abstract

Intravascular stents of various designs are currently in use to restore patency in atherosclerotic coronary arteries and it has been found that different stents have different in-stent restenosis rates. It has been hypothesized that the level of vascular injury caused to a vessel by a stent determines the level of restenosis. Computational studies may be used to investigate the mechanical behaviour of stents and to determine the biomechanical interaction between the stent and the artery in a stenting procedure. In this paper, we test the hypothesis that two different stent designs will provoke different levels of stress within an atherosclerotic artery and hence cause different levels of vascular injury. The stents analysed using the finite-element method were the S7 (Medtronic AVE) and the NIR (Boston Scientific) stent designs. An analysis of the arterial wall stresses in the stented arteries indicates that the modular S7 stent design causes lower stress to an atherosclerotic vessel with a localized stenotic lesion compared to the slotted tube NIR design. These results correlate with observed clinical restenosis rates, which have found higher restenosis rates in the NIR compared with the S7 stent design. Therefore, the testing methodology outlined here is proposed as a pre-clinical testing tool, which could be used to compare and contrast existing stent designs and to develop novel stent designs.

Keywords: Coronary stent; Finite-element method; Restenosis; Vascular injury; Arterial-wall mechanics

1. Introduction

Many clinical studies have been carried out to investigate the performance of cardiovascular stents and it has been found that different stents have different in-stent restenosis rates (McClean and Eigler, 2002; Colombo et al., 2002) with in-stent restenosis found to occur in as many as 20–50% of stented vessels (Grewe et al., 2000). Numerous computational studies have been carried out to investigate the expansion and mechanical behaviour of different stent designs; both balloon-expanding stent designs (Dumoulin and Cochelin, 2000; Etave et al., 2001; Tan et al., 2001; Migliavacca et al., 2002; Chua et al., 2003; Petrini et al., 2004) and nitinol self-expanding stents (Whitcher, 1997). However, very few analyses have been performed on the interaction between the stent and the artery, even though vascular injury has been hypothesized as the stimulus for the formation of occlusive intimal hyperplasia and eventual restenosis (Edelman and Rogers, 1998). In fact, vascular injury caused to a vessel by the implantation of a stent, whether defined by the depth of penetration of the stent wires or by an aggressiveness score, has consistently been found to determine the degree of restenosis (Schwartz and Holmes, 1994; Arakawa et al., 1998; Hoffman et al., 1999) and restenosis is therefore strongly linked to stent design (Rogers and Edelman, 1995; Kastrati et al., 2000).

In recent years, drug-eluting stents have emerged as an alternative to bare metal stents and are coated in an

*Corresponding author. Tel.: +353-1-608-1383; fax: +353-1-679-5554.
E-mail address: pprender@tcd.ie (P.J. Prendergast).
URL: http://www.biomechanics.ie.

0021-9290/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jbiomech.2004.07.022

anti-proliferative drug to prevent in-stent restenosis. Although, these stents have shown much promise it is still generally accepted that the optimal approach to coronary revascularization still lies in further developments in both stent design and drug-eluting stents (Lepor et al., 2002). Rogers et al. (1999) used the finite-element method to carry out a 2D analysis to investigate balloon–artery interactions during stent placement and showed that factors such as the balloon-inflation pressures, stent–strut openings and balloon compliance can influence the contact stresses between the balloon and the arterial tissue within the stent–struts and hence vessel injury. However, their study was limited to a 2D analysis and furthermore used linear elastic material properties to model the arterial tissue. A study of the arterial tissue within repeating units of different commercially available stent designs has been reported by Prendergast et al. (2003); they reported tissue prolapse and arterial wall stresses; however stent–artery contact was not simulated in that analysis nor were the models fully three dimensional (3D) in so far as only one repeating unit of each stent design was modelled. A fully 3D model has been developed by Auricchio et al. (2001), to look at an improvement to a stent design; however, the arterial tissue stresses were not reported. The most detailed numerical model to-date of a cardiovascular intervention is that by Holzapfel et al. (2002). They have developed a 3D model of a harvested cadaveric vessel using the finite-element method. The stresses induced within the vessel for a balloon angioplasty and a Palmaz–Schatz stenting procedure were determined. However, the localized stresses around the stent struts, i.e., the stresses most likely to provoke in-stent restenosis, were not computed and consequently it would not be possible to determine differences in the level of vascular injury as a function of stent design from their study.

In this paper, we test the hypothesis that two different stent designs will provoke different levels of stress in the vascular wall. The stents analysed were the S7 (Medtronic AVE, Minnesota, USA) and the NIR (Boston Scientific, Massachusetts, USA) stent designs. If this hypothesis is confirmed, and if the two stents also have significantly different restenosis rates, the study would support the use of computer-based finite-element analysis as a pre-clinical testing methodology to analyse the biomechanical attributes of cardiovascular stents.

2. Materials and methods

A finite-element analysis requires the geometry and material properties of the stent and blood vessel and appropriate loading conditions to simulate the stenting procedure, as described below. The finite-element software used was MSC Marc/Mentat (Santa Ana, CA, USA).

2.1. Model geometry

The 3D geometry of the repeatable units of the fully expanded 3.5 mm diameter NIR and S7 stents was determined using a coordinate measurement technique reported earlier (Prendergast et al., 2003). The thickness of the struts was 0.1 mm. Using the repeating unit geometry of each stent design, solid models of the full stents were generated. The solid models generated were of the stents in a planar state, i.e., the geometry of the stents if they were cut open longitudinally and flattened out. The stent solid models was then meshed and 'wrapped' into a cylindrical shape by transferring the nodal coordinates from a Cartesian coordinate system into a cylindrical coordinate system. In this way FE meshes were generated for each stent design as shown in Fig. 1. The two stent designs differed greatly; the NIR is a slotted tube laser-cut stent with 7 crowns whilst the S7 is a modular stent with a circular cross-section, 10 crowns and welded joints.

The atherosclerotic coronary artery was modelled as an idealized vessel and represented by a cylinder with outside diameter of 4 mm and had a localized crescent-shaped axisymmetric stenosis with minimum lumen diameter of 2 mm, see Fig. 2. The plaque corresponds to a maximum stenosis of 56% of the proximal and distal lumen cross-sectional area.

The adaptive meshing capability within Marc/Mentat was used in the models for the arterial tissue to allow the mesh to adapt and refine at contact areas. This enabled the elements in the region of highest stress gradients to subdivide and the finer mesh allowed for more accurate stress and strain evaluation in critical regions.

2.2. Material properties

The two materials of the artery wall, arterial tissue and stenotic plaque, were modelled using a 5-parameter third-order Mooney–Rivlin hyperelastic constitutive equation. This has been found to adequately describe the non-linear stress-strain relationship of elastic arterial tissue (Lally and Prendergast, 2003). The general polynomial form of the strain energy density function in terms of the strain invariants, given by Maurel et al. (1998) for an isotropic hyperelastic material is

$$W(I_1, I_2, I_3) = \sum_{i,j,k=0}^{\infty} a_{ijk}(I_1 - 3)^i(I_2 - 3)^j(I_3 - 3)^k, \quad a_{000} = 0, \tag{1}$$

where W is the strain-energy density function of the hyperelastic material, I_1, I_2 and I_3 are the strain invariants and a_{ijk} are the hyperelastic constants. If the

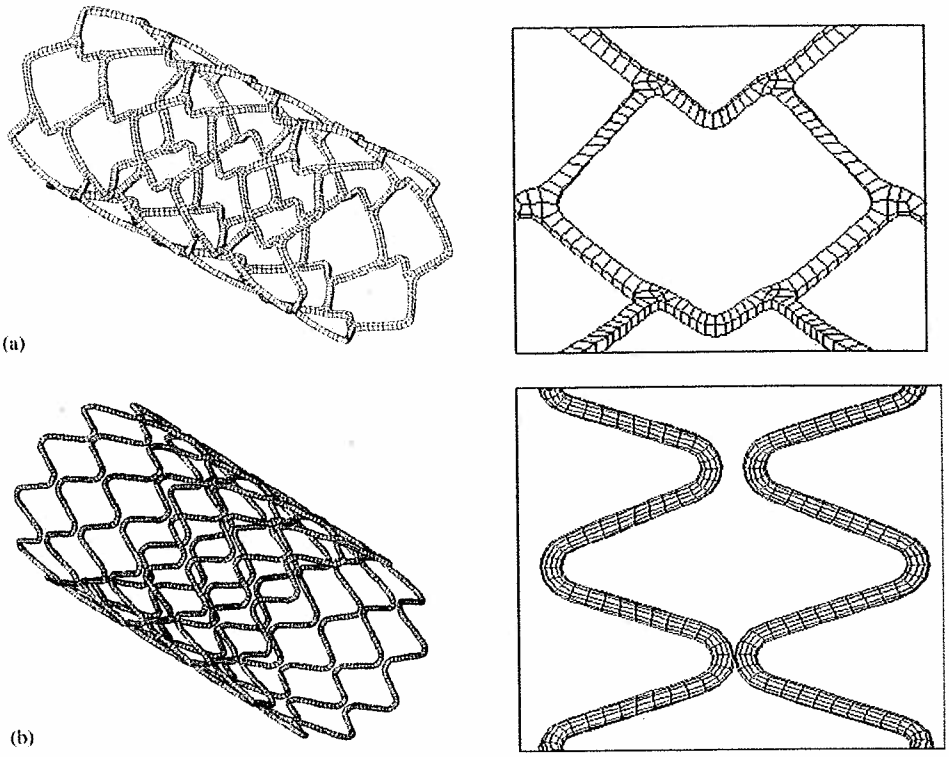

Fig. 1. Finite-element meshes of the fully expanded stents and exploded views of one repeating unit; (a) NIR stent and (b) S7.

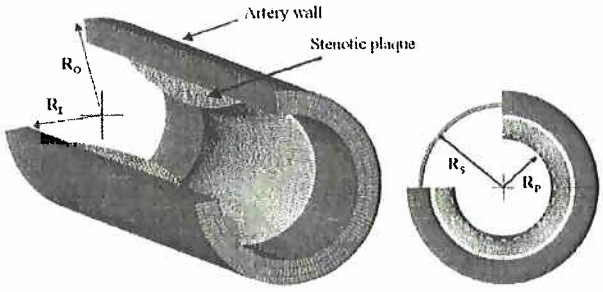

Fig. 2. Atherosclerotic coronary vessel geometry; artery outer radius, $R_0 = 2$ mm, Non-stenosed artery inner radius, $R_I = 1.5$ mm, stenosis inner radius, $R_P = 1$ mm, stent radius, $R_S = 1.75$ mm.

principal stretches of the material are denoted λ_1, λ_2 and λ_3, then the strain invariants for the material may be defined as

$$I_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2, \tag{2a}$$

$$I_2 = \lambda_1^2\lambda_2^2 + \lambda_1^2\lambda_3^2 + \lambda_2^2\lambda_3^2, \tag{2b}$$

$$I_3 = \lambda_1^2\lambda_2^2\lambda_3^2. \tag{2c}$$

Arterial tissue may be taken as incompressible based on the results of previous studies (Carew et al.,1968; Dobrin and Rovick, 1969). $I_3 = 1$ for an incompressible material. The specific hyperelastic-constitutive model used to model the arterial tissue in this study is a specific form of Eq. (1) whereby the strain-energy density function is a third-order hyperelastic model suitable for an incompressible isotropic material and has the form given in Eq. (3) (Mooney, 1940).

$$W = a_{10}(I_1 - 3) + a_{01}(I_2 - 3) + a_{20}(I_1 - 3)^2 + a_{11}(I_1 - 3)(I_2 - 3) + a_{30}(I_1 - 3)^3. \tag{3}$$

Using Eq (3) the stress components can be obtained by differentiating the strain-energy density function, W, with respect to the corresponding strain components (Humphrey, 2002).

The arterial tissue material model was determined by fitting to data from uniaxial and equibiaxial tension tests of human femoral arterial tissue. The uniaxial and equibiaxial experimental and hyperelastic material model data are shown in Fig. 3. More details of the determination of the experimental data and this hyperelastic-material model are given in Prendergast et al. (2003). The hyperelastic constitutive model used to represent the plaque tissue in the vessel with a localized stenotic lesion was determined by fitting to published data for human calcified plaques (Loree et al., 1994), see Fig. 4. Table 1 summarizes the constants used for the hyperelastic constitutive equations to define the two material models. The stent material was modelled as linear elastic 316L stainless steel ($E = 200$ GPa, $\nu = 0.3$).

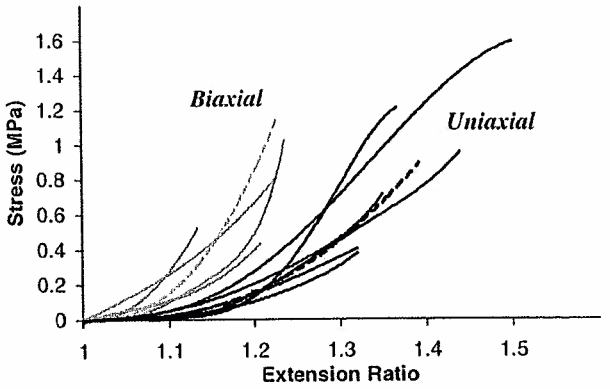

Fig. 3. Human femoral arterial tissue properties (solid lines) and the mechanical properties of the hyperelastic-material model for arterial tissue (dashed lines) (Prendergast et al., 2003).

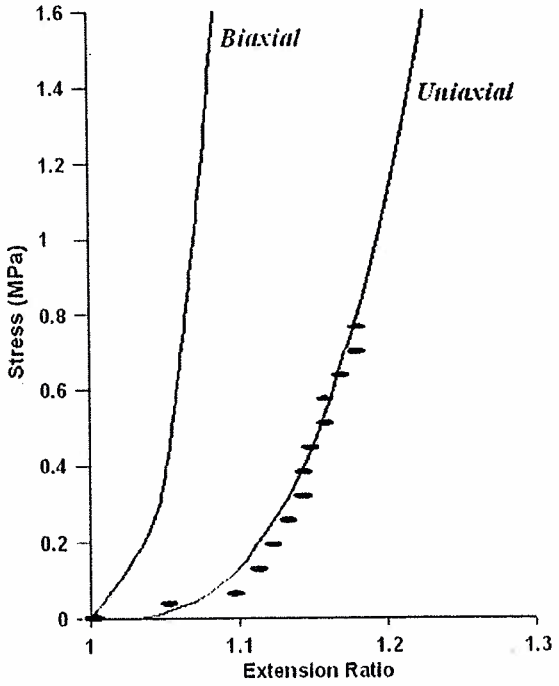

Fig. 4. Human calcified plaque properties (data points), adapted from Loree et al. (1994) (with permission), and the mechanical properties of the hyperelastic material model for plaque tissue (solid lines).

Table 1
Hyperelastic constants to describe the arterial tissue (Prendergast et al., 2003) and stenotic plaque non-linear elastic behaviour

	Arterial wall tissue (kPa)	Stenotic plaque tissue (kPa)
a_{10}	18.90	−495.96
a_{01}	2.75	506.61
a_{20}	85.72	1193.53
a_{11}	590.43	3637.80
a_{30}	0	4737.25

The parameters describe a Mooney–Rivlin model of the form given in Eq. (1).

2.3. Boundary conditions

The loading and restraint conditions were applied to the stent/artery construct in two steps. It involved use of the feature that exists in Marc/Mentat (and many other finite-element codes as well) that allows elements to be activated and deactivated during an analysis (called 'element birth and death'). In the first step, the stent elements were deactivated and the vessel was expanded to a diameter greater than that of the expanded stent by applying a sufficient internal pressure to the vessel (13 MPa). In the second step, the elements of the stent were activated and the pressure on the inner lumen of the artery was gradually reduced to a value of 13.3 kPa, corresponding to mean blood pressure of 100 mmHg. Due to the elastic nature of the hyperelastic arterial tissue the vessel contracted around the stent with the stent behaving as a scaffold within the vessel. Frictionless contact between the stent and the artery was assumed.

The contact algorithm implemented in marc/mentat was the direct constraint method. In this procedure, the motion of the bodies are tracked, and when contact occurs, direct constraints are placed on the motion using boundary conditions—both kinematic constraints on transformed degrees of freedom and nodal forces. Deformable–deformable contact was used to describe the contact between the two contact bodies, i.e., the stent and the artery. Both contact bodies were mathematically defined as analytical (NURB) surfaces. This leads to a more accurate solution because the normal to the contact surface is recalculated each iteration based upon the current surface position.

A longitudinal stretch of 1.2 was applied to the artery in an attempt to simulate the longitudinal tethering observed on coronary arteries in vivo (Weizsacker et al., 1983; Ogden and Schulze-Bauer, 2000). Axial restraints were applied to one end of the vessel. During the analysis the stent was restrained at one node in the circumferential direction to prevent rigid body rotations. Because of cyclic symmetry it was not necessary to model the entire stented vessel but rather only segments of the stented artery had to be modelled. Using the cyclic symmetry capability in Marc/Mentat, the nodes on the two cyclically symmetrical faces were coupled or tied. This allows out of plane motion (unlike planar symmetry constraints) and was therefore valid for representing a cyclically repeating segment of the stented vessel. Planar symmetry constraints cannot accurately model a cyclically repeating segment of a stenting procedure since the arterial geometry and the stent geometry in contact are not uniform in the axial direction. The NIR stent was represented by a cyclically repeating one-seventh segment whilst the S7 could only be represented by half-cyclic symmetry due to the position of the welds on the stent.

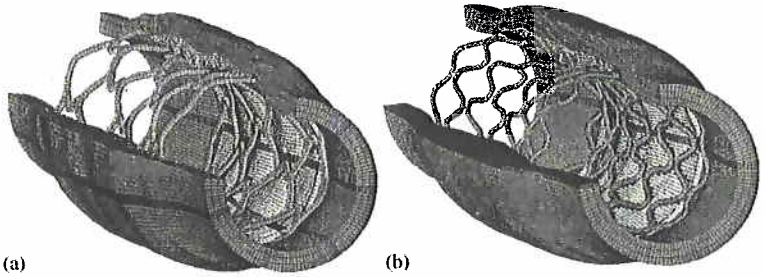

Fig. 5. The deformation of the artery, stenotic material and stent for (a) the NIR stent and (b) the S7 stent (one quarter of the artery and stenosis removed for viewing).

The element and node number used to represent the geometry of the two stenting simulations differed greatly as a result of the cyclic symmetry constraint applied. The one-seventh segment of the NIR stent was adequately represented by 125 elements and 470 nodes. For the half model of the S7, 5040 elements and 9021 nodes were necessary to model the circular cross-section of the stent. Although the mesh density used for the plaque and artery were the same in each model the number of elements differed since only one-seventh of the artery was represented in the NIR simulations whilst half of the artery had to be defined in the simulation of the S7 stenting procedure. This corresponded to 11,460 elements and 14,154 nodes for the NIR stenting procedure simulation and 40,040 elements and 47,783 nodes for the S7.

3. Results

The adaptive meshing incorporated into the simulations resulted in an increase in the number of elements and nodes defining the hyperelastic artery and plaque materials in both stenting simulations. The final number of elements that defined the artery was 22,072 (30,547 nodes) and 60,354 elements (80,293 nodes) in the NIR and S7 simulations, respectively.

The finite-element models predicted that both stents restored patency to the stenosed vessels, see Fig. 5a and b. As shown in Fig. 5a and b, the tissue drapes between the repeating units of the stents. Quantifying this, we find that the maximum tissue prolapse between the stent–struts to be 0.056 mm in the S7 stent compared with 0.124 mm for the NIR stent in the stenotic vessel. The contact area between the stent and the artery was 13.9 mm^2 for the NIR stent and 11.3 mm^2 the S7 stent.

The stresses induced within each stented vessel differed with a larger volume of highly stressed vascular wall predicted for the NIR stent, see Figs. 6 and 7. By analysing the volumes of the material stressed at different stress levels it was found that very high tensile stresses (>4 MPa) occurred in 21% of the artery stented with the NIR stent as compared to only 4% with the S7, see Fig. 7 for detailed results.

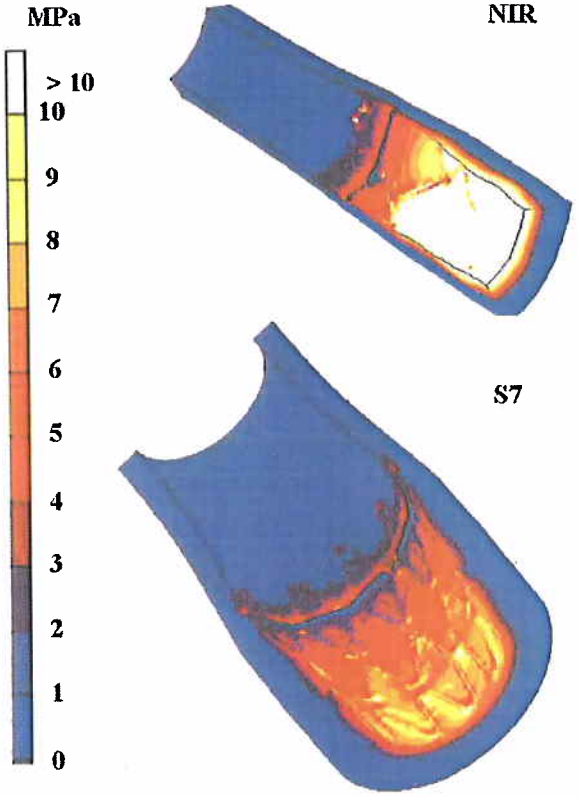

Fig. 6. Maximum principal stresses in atherosclerotic vessels stented with NIR and S7 stent. For symmetry reasons only 1/7 of the NIR and 1/2 of the S7 needs to be modelled.

Radial retraction was observed in the two stents as a result of the radial compressive forces exerted by the artery on the stents. This is to be expected due to bending of the stent struts and continued until equilibrium was reached between the radial strength of the stents and the radial compressive forces exerted by the artery. The retraction was found to be greater in the S7 compared with the NIR, see Fig. 8. The final lumen diameter corresponded to a final stenosis of 14% for the

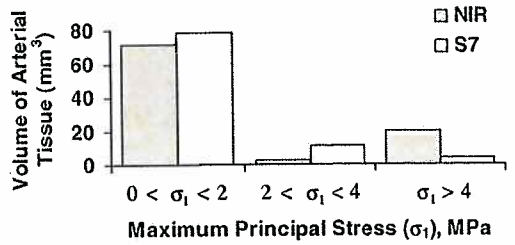

Fig. 7. Maximum principal stress volumes for the arterial tissue in the atherosclerotic vessel stented with an S7 and NIR stent.

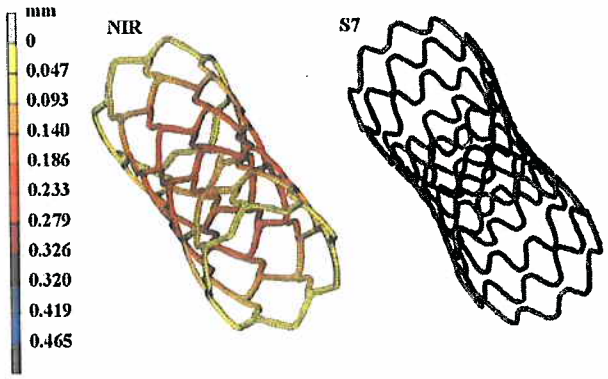

Fig. 8. Stent radial retraction in the models of the stented vessels.

NIR and 23% for the S7 stent, relative to the initial proximal and distal lumen area (i.e. the lumen area with a radius of 1.5 mm). However, the lumen cross-section was altered as a result of the axial stretch applied. As a result, the final lumen area at the stenosis corresponded to 8% increase in the lumen area, relative to the final proximal and distal lumen cross-sectional area in the NIR stenting simulation. It corresponded to 4% reduction (stenosis) in the final lumen cross-sectional area proximal and distal to the stenosis in the vessel stented with the S7 stent.

4. Discussion and conclusions

For a vessel with a localized stenotic lesion, based on the stresses induced in the vessel wall in these simulations, it is expected that the S7 would cause less vascular injury than the NIR. The lower volume of tissue stressed to high levels with the S7 stent compared to the same idealized geometry stented with the NIR made from the same material, can be attributed to the greater conformability of the S7 stent to the inner lumen geometry of the vessel. This includes the greater radial retraction observed in the S7 at the site of the vessel stenosis, see Fig. 8. By retracting, the stent maintains the lower stresses on the vessel; however the S7 maintains sufficient patency and superior scaffolding properties (0.056 mm maximum tissue prolapse compared with 0.124 mm for the NIR stent). In fact this value of maximum tissue prolapse is also very low compared with other stents designs (BeStent 2, *Medtronic AVE*; VELOCITY, *Cordis*; TETRA, *Guidant*), in which the maximum tissue prolapse within a repeatable stent unit of each of these designs has been determined in an earlier study (Prendergast et al., 2003).

Stent retraction is measured by the radial displacement of the stent; however, the tissue prolapse is tissue protrusion between the stent–struts and it defines the scaffolding properties of the stent. These results illustrate the coupling that exists between the stresses imposed on the vessel wall and the radial retraction of the stent. The radial retraction observed here is exaggerated as a result of the method used to simulate the stenting procedure, i.e., an expansion of the artery past the stent and the subsequent collapse of the artery around the stent. However, the simulations illustrate that if the two stent designs analysed were deployed using the same pressure in the same vessel that the NIR stent would induce higher stresses in the vessel wall. Clearly, an optimum stent design should retract sufficiently to prevent overstressing the vessel wall but still maintain patency of the vessel and plaque scaffolding. In fact, taking account of the differences in magnitude of radial retraction and tissue prolapse for the two stent designs, the minimum lumen diameter is predicted to be 2.63 and 2.79 mm at the vessel stenosis for the S7 and NIR stent, respectively. These correspond to 8% increase in the stenosis lumen area for the NIR stent and 4% reduction in the stenosis lumen area for the S7, relative to the final proximal and distal lumen area of the stented vessel. It is clear that the marginally higher lumen diameter achieved by the NIR stent is at the expense of large areas of considerably higher stress. These stresses may provoke a greater response to injury by the vessel wall and ultimately restenosis. This demonstrates the high risks associated with choosing an oversized rigid stent design as compared to the use of the more flexible S7 stent.

The clinical angiographic restenosis rate reported for the NIR stent is 19% at 6-month follow-up (Rutsch et al., 2000), and 19.3% at 9-month follow-up (Baim et al., 2001). The angiographic restenosis rate reported for the S7 stent at 6-month follow-up is 10.1% (Medtronic DISTANCE trial). The results of this study offer an explanation for this lower restenosis rate when compared with the NIR stent; the S7 stent would cause less vascular injury to the stented vessel and therefore would be expected to have a lower restenosis rate than the NIR stent whilst maintaining superior scaffolding properties than the NIR stent. It should also be noted that the S7 achieves high patency (only 4% stenosis) and excellent scaffolding whilst also having a lower stent/artery contact area (11.3 mm^2 as compared to 13.9 mm^2 for

the NIR). Maintaining the metal/tissue contact area low also reduces the thrombotic response of the vessel to the presence of a foreign material (Rogers and Edelman, 1995).

The main limitation of this study is that the arteries in which the stents are implanted are an idealized representation of stenosed coronary arteries. It is hypothesized, however, that the tortuosity of a realistic coronary artery model would only serve to further demonstrate the lower stresses generated by a flexible stent that can conform well to the vessel curvature relative to a stiffer stent. A more tortuous arterial geometry might also show that a rigid stent would cause even further high-stress concentrations and hence vascular injury at the ends of the stent, which could embed in the artery wall due to the relative non-conformability of the stent.

No rupture or damage mechanism has been incorporated into our plaque model. The high stresses observed in the calcified plaque are high enough that fracture could occur in this relatively brittle material. An analysis of the fracture process of the plaque is, however, beyond the scope of the present study. This study is currently being extended to develop a computational model of the restenosis mechanism using the stresses induced within the artery wall as a damage stimulus for the growth of restenotic tissue (Lally et al., 2004).

Finally, the process of stent expansion is not modelled in our simulations. This limits the study since it cannot be used to analyse the shearing force that an expanding stent could impose on an artery. In this respect, the approach used in this paper is suitable for studies that aim to look at the influence of stent placement on vessel wall stresses and stent-induced vascular injury after stent deployment since the stent geometry has been obtained from a stent in its expanded state.

The methodology described in this paper is proposed as a method to compare and analyse existing stent designs and can now also be used to develop new stent designs. Since this study already shows that stress predictions can be correlated with in-stent restenosis, it would be worthwhile to develop finite-element models of realistic vessel geometries, which can be obtained from Intravascular Ultrasound (IVUS) imaging. By determining full 3D patient specific geometries pre-stenting it may be possible to choose a stent design based on the patient's specific coronary artery stenosis geometry and thereby optimize the outcome of stenting procedures.

Acknowledgements

Project funded by an Applied Research Grant awarded by Enterprise Ireland to Medtronic Vascular, Galway, Ireland, and the Centre for Bioengineering, Trinity College, Dublin, Ireland, under the Programme for Research in Third Level Institutions, administered by the HEA.

References

Arakawa, K., Isoda, K., Sugiyabu, Y., Fukuda, M., Nishizawa, K., Shibuya, T., Nakamura, H., 1998. Intimal proliferation after stenting reflected by increased stent-to-vessel cross-sectional area ratio: serial intravascular ultrasound study. Journal of Cardiology 32, 379–389.

Auricchio, F., Di Loreto, M., Sacco, E., 2001. Finite-element analysis of a stenotic artery revascularization through a stent insertion. Computer Methods in Biomechanics and Biomedical Engineering 4, 249–263.

Baim, D.S., Cutlip, D.E., O'Shaughnessy, C.D., Hermiller, J.B., Kereiakes, D.J., Giambartolomei, A., Katz, S., Lansky, A.J., Fitzpatrick, M., Popma, J.J., Ho, K.K.L., Leon, M.B., Kuntz, R.E., NIRVANA Investigators, 2001. Final results of a randomized trial comparing the NIR stent to the Palmaz–Schatz stent for narrowings in native coronary arteries. American Journal of Cardiology 87, 152–156.

Carew, T.E., Vaishnav, R.N., Patel, D.J., 1968. Compressibility of the arterial wall. Circulation Research 22, 61–68.

Chua, S.N.D., MacDonald, B.J., Hashmi, M.S.J., 2003. Finite element simulation of stent and balloon interaction. Journal of Materials Processing Technology 143, 591–597.

Colombo, A., Stankovic, G., Moses, J.W., 2002. Selection of coronary stents. Journal of the American College of Cardiology 40, 1021–1033.

Dobrin, P.B., Rovick, A.A., 1969. Influence of vascular smooth muscle on contractile mechanics and elasticity of arteries. American Journal of Physiology 217, 1644–1651.

Dumoulin, C., Cochelin, B., 2000. Mechanical behaviour modelling of balloon-expandable stents. Journal of Biomechanics 33, 1461–1470.

Edelman, E.R., Rogers, C., 1998. Pathobiologic responses to stenting. American Journal of Cardiology 81, 4E–6E.

Etave, F., Finet, G., Boivin, M., Boyera, J.-C., Rioufol, G., Thollet, G., 2001. Mechanical properties of coronary stents determined by using finite element analysis. Journal of Biomechanics 34, 1065–1075.

Grewe, P.H., Deneke, T., Machraoui, A., Barmeyer, J., Muller, K.-M., 2000. Acute and chronic tissue response to coronary stent implantation: pathologic findings in human specimens. Journal of the American College of Cardiology 35, 157–163.

Hoffman, R., Mintz, G.S., Mehran, R., Kent, K.M., Pichard, A.D., Satler, L.F., Leon, M.B., 1999. Tissue proliferation within and surrounding Palmaz–Schatz stents is dependent on the aggressiveness of the stent implantation technique. American Journal of Cardiology 83, 1170–1174.

Holzapfel, G.A., Stadler, M., Schulze-Bauer, C.A.J., 2002. A layer-specific three-dimensional model for the simulation of balloon angioplasty using magnetic resonance imaging and mechanical testing. Annals of Biomedical Engineering 30, 753–767.

Humphrey, J.D., 2002. Cardiovascular Solid Mechanics. Cells, Tissues and Organs. Springer, New York.

Kastrati, A., Dirschinger, J., Boekstegers, P., Elezi, S., Schühlen, H., Pache, J., Steinbeck, G., Schmitt, C., Ulm, K., Neumann, F.-J., Schömig, A., 2000. Influence of stent design on 1-year outcome after coronary stent placement: a randomized comparison of five stent types in 1,147 unselected patients. Catheterization and Cardiovascular Interventions 50, 290–297.

Lally, C., Prendergast, P.J., 2003. An investigation into the applicability of a Mooney–Rivlin constitutive equation for modelling vascular tissue in cardiovascular stenting procedures. In:

Proceedings of the International Congress on Computational Biomechanics. Zaragoza, Spain, pp. 542–550.

Lally, C., Dolan, F., Prendergast, P.J., 2004. A computational model of in-stent restenosis in response to mechanical stress. In: Proceedings of the 10th Annual Conference of the Section of Bioengineering of the Royal Academy of Medicine in Ireland. Limerick, Ireland, p. 3.

Lepor, N.E., Madyoon, H., Kereiakes, D., 2002. Effective and efficient strategies for coronary revascularization in the drug-eluting stent era. Reviews in Cardiovascular Medicine 3, S38–S50.

Loree, H.M., Grodzinsky, A.J., Park, S.Y., Gibson, L.J., Lee, R.T., 1994. Static and circumferential tangential modulus of human atherosclerotic tissue. Journal of Biomechanics 27, 195–204.

Maurel, W., Wu, Y., Magnenat Thalmann, N., Thalmann, D., 1998. Biomechanical Models for Soft-Tissue Simulation. Springer, Berlin.

McClean, R., Eigler, N.L., 2002. Stent design: implications for restenosis. Reviews in Cardiovascular Medicine 3, S16–S22.

Medtronic DISTANCE trial: whitepaper reporting on the direct stenting with angiographic and clinical evaluation of the S7 (DISTANCE) trial: medtronic AVE, UC200203607EE 6M 5/02.

Migliavacca, F., Petrini, L., Colombo, M., Auricchio, F., Pietrabissa, R., 2002. Mechanical behavior of coronary stents investigated through the finite element method. Journal of Biomechanics 35, 803–811.

Mooney, M., 1940. A theory of large elastic deformation. Journal of Applied Physics 11, 582–592.

Ogden, R.W., Schulze-Bauer, C.A.J., 2000. Phenomenological and structural aspects of the mechanical response of arteries. In: Casey, J., Bao, G. (Eds.), Mechanics in Biology. BED 46, pp. 125–140.

Petrini, L., Migliavacca, F., Auricchio, F., Dubini, G., 2004. Numerical investigation of the intravascular coronary stent flexibility. Journal of Biomechanics 37, 495–501.

Prendergast, P.J., Lally, C., Daly, S., Reid, A.J., Lee, T.C., Quinn, D., Dolan, F., 2003. Analysis of prolapse in cardiovascular stents: a constitutive equation for vascular tissue and finite element modelling. ASME Journal of Biomechanical Engineering 125, 692–699.

Rogers, C., Edelman, E.R., 1995. Endovascular stent design dictates experimental restenosis and thrombosis. Circulation 91, 2995–3001.

Rogers, C., Tseng, D.Y., Squire, J.C., Edelman, E.R., 1999. Balloon–artery interactions during stent placement. A finite element analysis approach to pressure, compliance, and stent design as contributors to vascular injury. Circulation Research 84, 378–383.

Rutsch, W., Kiemeneij, F., Colombo, A., Macaya, C., Guermonprez, J.-L., Grip, L., Hamburger, J., Umans, V., Gotsman, M., Almagor, Y., Morice, M.-C., Garcia, E., Chevalier, B., Erbel, R., Cobaugh, M., Morel, M.-A., Serruys, P.W., 2000. Clinical and angiographic results with the NIR stent: First International NIR Endovascular Stent Study (FINESS-II). International Journal of Cardiovascular Interventions 3, 143–150.

Schwartz, R., Holmes, D.R., 1994. Pigs, dogs, baboons, and man; lessons in stenting from animal studies. Journal of Interventional Cardiology 7, 355–368.

Tan, L.B., Webb, D.C., Kormi, K., Al-Hassani, S.T.S., 2001. A method for investigating the mechanical properties of intracoronary stents using finite element numerical simulation. International Journal of Cardiology 78, 51–67.

Weizsacker, H.W., Lambert, H., Pascale, K., 1983. Analysis of the passive mechanical properties of rat carotid arteries. Journal of Biomechanics 16, 703–715.

Whitcher, F.D., 1997. Simulation of in vivo loading conditions of nitinol vascular stent structures. Computers and Structures 64, 1005–1011.

EXHIBIT C

Medical Device Recalls Class 2 Recall

Date Recall Initiated	April 01, 2003
Date Posted	April 22, 2003
Recall Number	Z-0775-03
Product	Guidant Multi-Link Vision Coronary Stent System Catalog Numbers: 30 different catalog numbers have been listed. The firm indicates that total numbers of devices subject to this removal are being defined.
Code Information	All lots are included in the action.
Recalling Firm/ Manufacturer	Guidant Corporation ACS 26531 Ynez Road Temecula , California 92591-4628
For Addition Information Contact	James C. McMahon, PhD 909-914-2298
Reason For Recall	Complaints that the stents are being dislodged from the delivery system.
Action	Information as an Advisory Notice was sent by facsimile to the Competent Authorities and to distributors on April 1 2003. Recall letters will be delivered

	by hand in most instances. . Firm Initiated recall is ongoing.
Quantity in Commerce	Estimated 7 to 9 thousand units
Distribution	No USA distribution, only to the countries of Australia, Austria, Belgium, Denmark, Finland, France, Germany, Greece, Italy, Lebanon, Netherlands, Norway, Poland, Portugal, Spain, Sweden, Switzerland, Tunisia, United Kingdom.

Medical Device Recalls
Class 2 Recall

See Related Information

Date Recall Initiated	May 07, 2003
Date Posted	May 22, 2003
Recall Number	Z-0862-03
Product	MULTI-LINK Pixel Coronary Stent System Size: 2.0 x 13 mm OTW Part Number: 1007830-13
Code Information	Lot 3021951
Recalling Firm/ Manufacturer	Guidant Corporation ACS 26531 Ynez Road Temecula , California 92591-4628
For Addition Information Contact	James C. McMahon 909-914-2298
Reason For Recall	Sterility compromised.
Action	The firm initially is notifying by letter dated May 6, 2003 and will plan visit follow-ups to collect quarantined product. . Firm Initiated recall is ongoing.
Quantity in Commerce	40

Distribution NATIONWIDE

Medical Device Recalls Class 2 Recall

See Related Information

Date Recall Initiated	July 15, 2003
Date Posted	August 01, 2003
Recall Number	Z-1075-03
Product	Guidant Multi-Link Zeta Coronary Stent System
Code Information	3050632 3060432 3060251 3051952 3052251 3060331 3051231 3051951 3052752 3052031 3051931 3050651 3052752 3060531 3060451 3050751 3052251 3051951 3050931 3050632 3052032 3060251 3051531 3053051 3051634 3051632 3053051 3051531 3052952 3051552 3050931 3052852 3060431 3060432 3050751 3052131 3051532 3052031 3051631 3050251 3043051 3050931 3051531 3051451 3052851 3051551 3051531 3041031
Recalling Firm/ Manufacturer	Guidant Corporation ACS 26531 Ynez Road Temecula , California 92591-4628
For Addition Information Contact	Michael Schwartz 909-914-2627

Reason For Recall	Potential loss of package sterility.
Action	Firm personnel in China have inspected all Chinese consignee end user inventories. Any units found to be defective have been removed and are currently in Guidant control. . Firm Initiated recall is ongoing.
Quantity in Commerce	Not stated
Distribution	China

EXHIBIT D

HHS *NEWS*

U.S. Department of Health and Human Services

P98-29
FOR IMMEDIATE RELEASE
October 8, 1998

FOOD AND DRUG ADMINISTRATION
Sharon Snider: 301-827-6242

Consumer Inquiries: 800-532-4440

BOSTON SCIENTIFIC ISSUES NATIONWIDE RECALL OF HEART STENT

Boston Scientific Corporation, headquartered in Natick, Mass., announced on October 5 that it has stopped distributing its NIR ON Ranger with Sox coronary stent delivery system and is voluntarily withdrawing the product from the market due to a serious risk of patient injury. The Sox system is one of two delivery systems marketed for the stent. The recall will be handled by the company's Maple Grove, Minn., facility.

The FDA considers the withdrawal to be a total product recall. FDA urges hospitals to immediately stop using this device because of potential risk to patients.

The product, launched in early August, was shipped to more than 200 hospitals and medical centers throughout the United States. Approximately 36,000 systems have been shipped and the company estimates 25,000 have been used.

The device is implanted in patients to help keep open previously blocked heart arteries after the blockage has been cleared. It has been popular with doctors because of its thinness and ease of manipulation, which allow it to be used in small or twisting coronary arteries.

The firm's decision to recall the product was based on their receipt of more than 100 reports of balloon leakage. The company has reported 26 injuries and one death to the FDA. The balloon is a key element in the coronary stent system. After the stent is positioned, the balloon is expanded and as it expands, it pushes the stent up against the plaque, the fatty tissue blocking the artery wall. The balloon is then deflated and withdrawn, leaving the stent permanently in place to prop open the blood vessel.

The company has stated that the reports of injury were likely attributed to a change in the manufacturing process that affected the balloon only. That change was not reviewed or approved by FDA's product review staff.

There are two delivery systems for the NIR ON Ranger: one with Sox and one without. As the firm recalls the NIR ON Ranger with Sox, the NIR ON Ranger coronary stent without Sox will continue to be available. The company has evaluated that system and indicated to FDA that it performs as specified and as labeled.

Hospitals with questions may contact the company at 1-888-724-6334.

FDA is disseminating additional information to physicians through health care professional organizations to alert them to the problem.

####

ATTENTION TV BROADCASTERS: Please use open caption for the hearing impaired.

FDA HOME PAGE

The following document is a copy of a **Press Release** from **Boston Scientific** releated to the Class I Medical Device Recall of the Boston Scientific Express^{2TM} (bare metal) Coronary Stent.

BOSTON SCIENTIFIC TO RECALL
ADDITIONAL CORONARY STENT SYSTEMS

Natick, MA (July 16, 2004) – Boston Scientific Corporation (NYSE: BSX) announced today that it is expanding its voluntarily worldwide recall to include certain additional units of its TAXUS^{TM} Express^{2TM} Paclitaxel-Eluting Coronary Stent Systems. The Company is also beginning a voluntary recall of certain units of its Express^{2TM} Coronary Stent Systems (bare metal stents). The Company has notified the U.S. Food and Drug Administration (FDA) and plans to notify officials in other affected countries.

On July 2, the Company announced the recall of approximately 200 TAXUS Express^2 Paclitaxel-Eluting Coronary Stent Systems, due to characteristics in the delivery catheters that have the potential to impede balloon deflation during a coronary angioplasty procedure. Since then, the Company has conducted further analysis and investigation of the TAXUS Express^2 (paclitaxel-eluting) and Express^2 (bare metal) stent systems, both of which share the same delivery catheter, and has identified additional production lots which may exhibit these characteristics. While the number of customer reports of balloon deflation difficulty is extremely small, patient safety is the Company's paramount concern, and therefore it has chosen to initiate this broader recall. Impeded balloon deflation can result in significant patient complications, including coronary artery bypass graft surgery and death. The Company has received reports of one death and 18 serious injuries associated with balloon deflation for the TAXUS stent system, and two deaths and 25 serious injuries associated with balloon deflation in the Express^2 (bare metal) stent system. The units being recalled were manufactured at the Company's Galway, Ireland and Maple Grove, Minnesota facilities.

The recall will involve approximately 85,000 TAXUS stent systems and approximately 11,000 Express^2 stent systems. Overall, the Company has shipped more than 500,000 TAXUS stent systems and more than 600,000 Express^2 stent systems. The recall does not affect the ExpressTM SD and LD biliary stent systems.

The Company implemented review of its manufacturing process, additional inspections, and an FDA-approved modification to the manufacturing process for these products. The current and future production are not expected to experience similar balloon deflation problems.

"Patient safety continues to be our highest priority," said Jim Tobin, President and Chief Executive Officer of Boston Scientific. "We have every confidence these products are safe and effective, and we expect that these measures will go a long way toward reducing the occurrence of these events. We regret

any disruption this recall may cause to physicians and their patients. We're fortunate that current TAXUS inventory levels will minimize service disruption in the United States, but we do expect some disruption internationally. We will continue to monitor the quality and performance of the affected products, and we will take appropriate action to ensure patient safety."

Today's action does not affect patients who have already received these stents, because the difficulty is with the delivery system and occurs at the time of insertion, not afterward.

Institutions with affected units will be receiving packages outlining the recall process and should immediately discontinue use of these units. Clinician and patient inquiries may be directed to Boston Scientific at 800-832-7822.

The Company expects that the recall will impact the financial results for the second quarter. On a preliminary basis, it is expected that the impact will include the reversal of sales related to the recalled products of approximately $45 million (pre-tax) and a write-down of inventory of approximately $50 million (pre-tax).

In light of today's announcement, the Company will postpone the announcement of its financial results for the second quarter, originally scheduled for Monday, July 19, so that it may finalize the adjustments necessitated by the recall. The Company plans to reschedule the call for Monday, July 26, at a time to be announced next week.

Boston Scientific officials will be discussing this press release with analysts on a conference call at 3:45 p.m. (ET) today. The Company will webcast the call to all interested parties through its website www.bostonscientific.com. Please see the website for details on how to access the webcast. The webcast will be archived and available for 10 days on the Boston Scientific website.

Boston Scientific is a worldwide developer, manufacturer and marketer of medical devices whose products are used in a broad range of interventional medical specialties. For more information, please visit: www.bostonscientific.com.

This press release contains forward-looking statements. The Company wishes to caution the reader that actual results may differ from those discussed in the forward-looking statements and may be adversely affected by, among other things, risks associated with the regulatory process, litigation, competitive product offerings and other factors described in the Company's filings with the Securities and Exchange Commission.

CONTACT: Milan Kofol
508-650-8569 (Office)
617-834-8595 (Mobile)
Investor Relations
Boston Scientific Corporation

Paul Donovan
508-650-8541 (Office)
508-667-5165 (Mobile)
Media Relations
Boston Scientific Corporation

Updated July 22, 2004
